ACTIVE IMMUNOTHERAPY OF METASTATIC RENAL CELL CARCINOMA USING AUTOLOGOUS DENDRITIC CELLS TRANSFECTED WITH AUTOLOGOUS RENAL TUMOR RNA

SCIENTIFIC ABSTRACT

The objective of this safety and feasibility study (Phase I) is to develop a clinically relevant and broadly applicable vaccine strategy for the treatment of patients with metastatic renal cell carcinoma. In particular, we propose to study the use of autologous dendritic cells (DC) transfected with autologous tumor RNA for their ability to induce significant levels of tumor specific T cells in renal cell carcinoma patients.

A large body of preclinical studies has shown that vaccinations with tumor RNA transfected dendritic cells can serve as a potent and widely applicable platform to elicit tumor specific CTL responses in cancer patients. Furthermore, we have demonstrated that DC generated from prostate cancer patients and transfected with a 'model RNA', namely PSA-RNA, can induce potent PSA responses *in vitro* and *in vivo* regardless of the cellular MHC composition, a fact, which will greatly expand the patient population eligible for this broadly applicable therapy. This immune response is ultimately hoped to reduce tumor burden and to prolong survival of cancer patients. RNA molecules are transitory in nature and RNA transcripts do not integrate into chromosomal DNA, thereby eliminating or greatly reducing the risks of insertional mutagenesis in eukaryotic cells.

The overall objective of this safety and feasibility trial is to evaluate this modality with respect to safety of clinical administration and induction of tumor specific T cell responses. Escalating doses of autologous progenitor derived DC transfected with renal tumor RNA will be administered in dose ranges feasible from a single leukapheresis procedure. The primary and secondary objectives of this study are:

a) Evaluate the safety and feasibility of escalated doses of renal tumor RNA transfected DC.

b) Evaluate the induction of tumor specific immune responses following tumor RNA transfected DC administration.

c) Monitor eventual clinical responses by measurable disease response criteria.

d) Develop a DC vaccination platform for patients with advanced or recurrent cancers.

It is hoped that this trial will set the stage for definitive trials designed to demonstrate a clinical benefit of active immunotherapy in patients with metastatic renal cell carcinoma using tumor RNA transfected DC vaccines by reducing cancer recurrence and metastasis.